学位論文の要旨

Lubiprostone Decreases the Small Bowel Transit Time by Capsule Endoscopy: An Exploratory, Randomised, Double-Blind, Placebo-Controlled 3-Way Crossover Study

（健常成人男性におけるルビプロストンによる胃・小腸通過時間への影響）
（-カプセル内視鏡を用いて-）

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Introduction:

Lubiprostone (Amitiza; Takeda Pharmaceuticals North America, Deerfield, IL) selectively activates the type-2 chloride channels in the apical membrane of the GI epithelium, inducing net fluid secretion. The proposed primary mechanism of action of lubiprostone in the gastrointestinal tract is increased chloride ion transport into the intestinal lumen by the drug caused by the opening of ClC-2, which results in increased intestinal secretion and accelerated mass transit [J. Cuppoletti et al., 2004. and A. Postgate et al., 2009.]. The aim of this study was to investigate the usefulness of lubiprostone for bowel preparation and as a propulsive agent in small bowel endoscopy.

Methods:

This was a randomized, double-blind, placebo-controlled, 3-way crossover study of subjects who volunteered to undergo CE. The subjects were 6 asymptomatic male volunteers (average age: 35.8 years; age range: 29–50 years). In all the subjects, the CE was performed with the PillCam SB2 CE system (Given Imaging Ltd.), and the images were viewed with the Rapid 5 Reader. The subjects were randomly assigned to receive a 24 μg tablet of lubiprostone 60 minutes prior to the capsule ingestion for CE and a placebo tablet 30 minutes before the capsule ingestion (L-P regimen), a placebo tablet 60 minutes prior to the capsule ingestion for CE and a 24 μg tablet of lubiprostone 30 minutes prior to the capsule ingestion (P-L regimen), or a placebo tablet 60 minutes prior to the capsule ingestion for CE and a placebo tablet again 30 minutes prior to the capsule ingestion (P-P regimen) . Each of the test conditions was separated by a washout period of at least 7 days.

All the study subjects were instructed to have a light breakfast and then clear liquids on the day prior to the CE. Furthermore, they were instructed to have nothing by mouth for at least 8 hours prior to the capsule ingestion for CE. All the CE images were read by two investigators (Masahiko Inamori and Mizue Matsuura), both of whom were blinded to the group allocation status of the

subjects. The small bowel examination was considered to be complete if the capsule had passed into the colon.

The quality of the capsule endoscopic images and the amount of water in the small bowel were assessed on 5-point scale. We used a 5-point scale (0–4) based on the percentage of the capsule images that were unimpaired by the presence of debris or dark luminal fluid (4, 100–80%; 3, 80–60%; 2, 60–40%; 1, 40–20%; 0, 20–0%). The average scores for 5min segments of the video were assessed from capsule entry into the proximal duodenum (0% of the SBTT) and for every 10% of the SBTT thereafter, with the score for the final segment recorded in the terminal ileum (100% of the SBTT).

Results:

The study was completed in six male subjects (mean age: 39.5 years; range: 29–50 years). No adverse events occurred during the study. The median GTT was 22.5 (9–160) minutes in the P-P regimen, 40 (4–122) minutes in the L-P regimen, and 57.5 (15–78) minutes in the P-L regimen (P = 0.846). The median SBTT was 178.5 (117–407)minutes in the P-P regimen, 122.5 (27–282) minutes in the L-P regimen, and 110.5 (11–331) minutes in the P-L regimen (P = 0.042). The median SBTT values for the L-P and P-L regimens were statistically significantly different from the SBTT in the P-P regimen.

The image quality score was 2.88 ± 1.35 in the P-P regimen, 3.56±0.56 in the L-P regimen, and 3.76±0.85 in the P-L regimen (P < 0.001). The amount of water in the small bowel was 1.66 ± 1.65 in the P-P regimen, 3.13 ± 1.64 in the L-P regimen, and 2.60 ± 1.29 in the P-L regimen (P < 0.01).

Discussion:

This study was designed to evaluate the effect of lubiprostone on the capsule transit time through the GI lumen and its effectiveness as a bowel preparation agent for improving the quality of capsule imaging of the small bowel. Lubiprostone improved the imaging quality of the small bowel as compared to placebo and also improved the SBTT. The GTT following administration of lubiprostone was similar to that after administration of placebo. Our findings differ from those of the study reported by Camilleri et al. 2006, who reported finding evidence of delayed gastric emptying following the administration of lubiprostone. The main side effect of lubiprostone was nausea, possibly related to delayed gastric emptying. Lubiprostone improved the SBTT as compared to placebo. Camilleri et al. showed lubiprostone decreased SBTT in 2006. In addition, lubiprostone has been shown to accelerate overall colonic transit without significantly changing the rate of emptying of the ascending colon [J. Cuppoletti et al., 2004.]. Our study shows that lubiprostone significantly decreases the SBTT and improves the visualization of the small bowel during CE. We also confirm that lubiprostone induces water secretion into the small bowel lumen by capsule endoscopy.

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論　文　目　録

主論文

“Lubiprostone Decreases the Small Bowel Transit Time by Capsule Endoscopy: An Exploratory, Randomised, Double-Blind, Placebo-Controlled 3-Way Crossover Study”

MizueMatsuura, Masahiko Inamori, Hiroki Endo, Tetsuya Matsuura, Kenji Kanoshima, Yumi Inoh, Yuji Fujita, Shotaro Umezawa, Akiko Fuyuki, Shiori Uchiyama, Takuma Higurashi, Hidenori Ohkubo, Eiji Sakai, Hiroshi Iida, Takashi Nonaka, Seiji Futagami, Akihiko Kusakabe, Shin Maeda, and Atsushi Nakajima.

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